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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,902	07/02/2002	Nikolai Vladimirovich Bovin	9286-7	7167

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EXAMINER

MAIER, LEIGH C

ART UNIT PAPER NUMBER

1623

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/019,902

Applicant(s)

BOVIN ET AL.

Examiner

Leigh C. Maier

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6,8-12,14-16,18,20,23,27 and 28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6,8-12,14-16,18,20,23,27 and 28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 December 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)            |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>8/5/02</u> . | 6) <input type="checkbox"/> Other: ____  |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election of CH<sub>4-m</sub> as the species "X" is acknowledged. As noted by Applicant, Applicant will be entitled to consideration of claims to additional species upon a finding of allowability of the present species.

Claims 1, 2, 4-6, 8, 10-12, 14-16, 18, 20, 23, 27, and 28 are generic. Claim 3 is sub-generic. Claim 9 is specific to the elected species.

### ***Information Disclosure Statement***

It is noted that the Applicant has submitted the references listed on the International Search Report for the PCT. However, these have not been listed on a separate form PTO-1449. In order for these references to be made of record in the instant prosecution, Applicant is required to submit such a form with a listing of the references for initialing by the examiner.

### ***Drawings***

The drawings are objected to because there appears to be a discrepancy in Figure 1. The elution profiles are labeled "n=0", n=1", etc. However the caption comprises a formula that does not contain the variable "n", only variables "m" and "x". It appears that "n" should be "m" or vice versa. Applicant is required to explain the apparent discrepancy or submit corrected drawings. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing

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sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Rejections - 35 USC § 112 – 2<sup>nd</sup> paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8, 10-12, 14-16, 18, 20, 23, 27, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The formula in the claims recites a moiety, B, which comprises, K, which in turn comprises  $(A^2-A^3)_k$ . By convention, when a formula such as  $(A^2-A^3)_k$  is used, it means "k  $(A^2-A^3)$ s in sequence" with all k  $(A^2-A^3)$ s being the same. For example, if k=5, and together  $(A^2-A^3)$  form a glycy radical,  $(A^2-A^3)_k$  would mean gly-gly-gly-gly-gly. It is noted that in the examples,

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there is a compound wherein all the ( $A^2-A^3$ )s are not the same. See Table 1, the fourth compound in the left column, wherein the ( $A^2-A^3$ )s are not all the same. It is further noted that this compound is not encompassed by the formula recited in the claims because  $k < 5$ . Therefore, it is not clear whether this is simply a reference compound or if is the type of compound Applicant contemplates as part of the invention, that is, all the ( $A^2-A^3$ )s do not have to be identical.

***Claim Rejections - 35 USC § 112 – 1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-12, 14-16, 18, 20, 23, 27, and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the examples disclosed in the specification that are described as forming aggregates and having utility in the inhibition of the influenza virus but not the full scope of compounds (limited to those wherein  $X=CH_{4-m}$  at this stage of examination) encompassed by the claims, does not reasonably provide enablement for the full scope of compounds embraced by the formula wherein  $X=CH_{4-m}$ . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- (1) The quantity of experimentation necessary (time and expense);
- (2) The amount of direction or guidance presented;
- (3) The presence or absence of working examples of the invention;
- (4) The nature of the invention;

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- (5) The state of the prior art;
- (6) The relative skill of those in the art;
- (7) The predictability or unpredictability of the art; and
- (8) The breadth of the claims.

The recited formula embraces a very extensive number of compounds, but the specification discloses a relatively small number of embodiments. In the compounds, the required characteristics are (1) four identical B moieties; (2)  $(A^2-A^3)=\text{gly}$ ; (3) k is at least 5; (3) a spacer is present; and (4) the R moiety is a small saccharide. These characteristics appear necessary, but not sufficient. See, for example the third entry in Table 1 at page 14. This compound has no increased activity over the monomer. See also the sixth entry in Table 7 at page 31. This compound does not form aggregates. A post-filing reference TUZIKOV et al (ChemBioChem, 2003) also discloses other compounds having the above characteristics but do not form aggregates or have any therapeutic advantage over the monomeric compounds. See page 151. These disclosures demonstrate great differences in compounds having relatively similar structure. See also, TUZIKOV, at the paragraph bridging pages 147 and 148. This indicates a high degree of unpredictability in the art.

There is no indication that compounds with an m value of less than 4 would have these advantageous aggregating properties. The discussion in TUZIKOV regarding the self-assembling patterns of these tetraantennary glycopeptides would suggest that they do not. See Figure 5 and discussion thereof.

Although the segment of B defined by  $(A^2-A^3)$  provides countless options, the examples are confined to glycine. TUZIKOV state that “[t]he unusual stability of the tectomer in aqueous media can be explained by the participation of all CO and NH glycine groups in H bonding in a

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highly cooperative manner. . .” See page 150, last paragraph. It appears that the glycopeptides comprising oligoglycyl “arms” may be a special sub-set within the recited compounds.

With regard to the preparation of these compounds, TUZIKOV describes difficulties encountered during the preparation of compounds wherein  $k$  is about 7 or greater that do not appear to be mentioned in the present specification. See page 148. It would appear that the method used in example 7 of the instant specification would give complete acylation.

In light of the forgoing, one of ordinary skill would require undue experimentation at great expense to be able to determine which of the countless compounds defined by the recited formula would have the necessary property of self-assembly (aggregation) making the useful for the treatment of influenza.

With regard to the therapeutic methods, the claims are drawn to the treatment of a broad group of diseases and disorders, but the only experimental data are *in vitro* tests for influenza. The basis for the increased activity of the tetraantennary compounds is purportedly providing multivalent active ingredient that can be arranged in a thermodynamically advantageous to optimize receptor interaction. First regarding influenza, the instant specification persuasively demonstrates increased therapeutic activity (based on *in vitro* data) for compounds having particular oligosaccharides and  $k$  values of about 5 to 7. However, the formula recites  $k$  values up to 100. Again, TUZIKOV notes the increased difficulty in preparing compounds with greater  $k$  values, but assuming for the sake of argument that these compounds can be *prepared* without undue experimentation and that they would be suitably soluble for preparation of pharmaceutical compositions, (not that the examiner concedes that the case has been made) it would appear unlikely that they would have the appropriate configuration to interact with the receptors

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advantageously. Furthermore, the treatment of other non-influenza diseases would be based on interaction with entirely different receptors with different structural characteristics. With so little guidance provided by the specification, it would require undue experimentation for one of ordinary skill to select which of the multitudinous compounds defined by the formula would have utility for which of the recited list of diseases and disorders.

*Examiner's hours, phone & fax numbers*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

*Leigh C. Maier*

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Patent Examiner  
September 3, 2004